The LIM protein Ajuba restricts the second heart field progenitor pool by regulating Isl1 activity.

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Public Summary:
The stabilization of Nkx2.5 by Ajuba may be involved in preventing cardiac progenitor cell overspecification

Scientific Abstract:
Morphogenesis of the heart requires tight control of cardiac progenitor cell specification, expansion, and differentiation. Retinoic acid (RA) signaling restricts expansion of the second heart field (SHF), serving as an important morphogen in heart development. Here, we identify the LIM domain protein Ajuba as a crucial regulator of the SHF progenitor cell specification and expansion. Ajuba-deficient zebrafish embryos show an increased pool of Isl1(+) cardiac progenitors and, subsequently, dramatically increased numbers of cardiomyocytes at the arterial and venous poles. Furthermore, we show that Ajuba binds Isl1, represses its transcriptional activity, and is also required for autorepression of Isl1 expression in an RA-dependent manner. Lack of Ajuba abrogates the RA-dependent restriction of Isl1(+) cardiac cells. We conclude that Ajuba plays a central role in regulating the SHF during heart development by linking RA signaling to the function of Isl1, a key transcription factor in cardiac progenitor cells.